

Figure 1

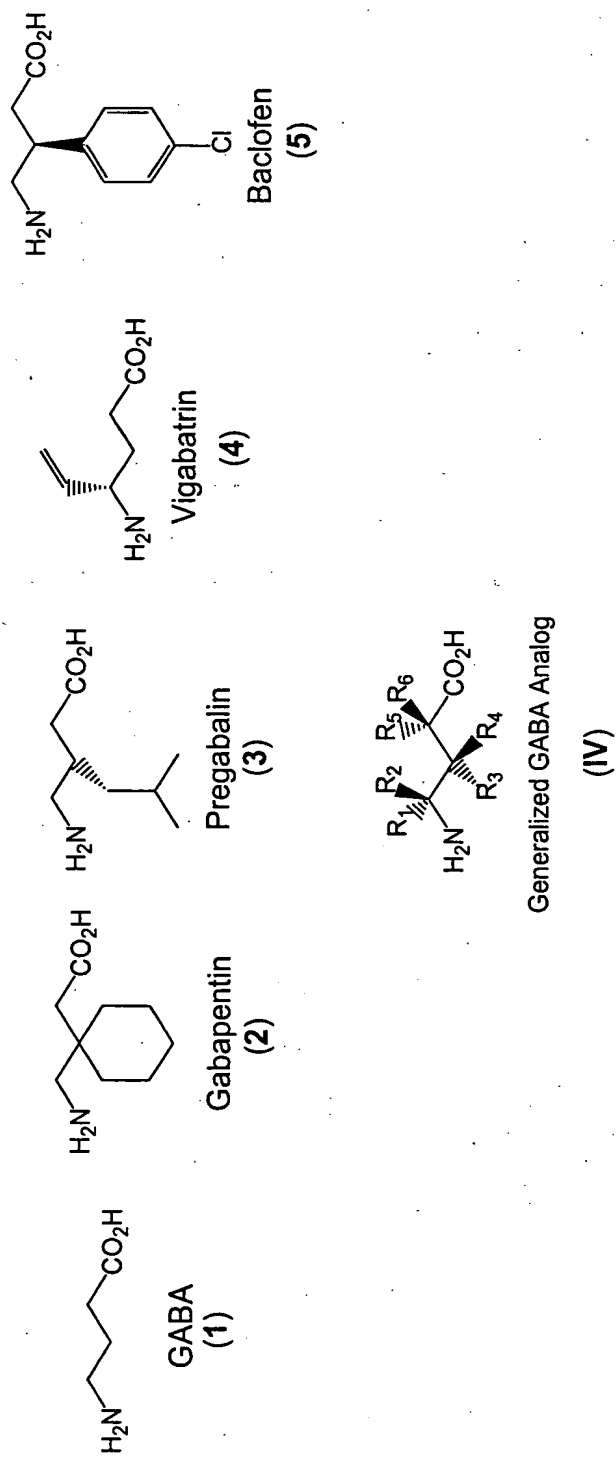
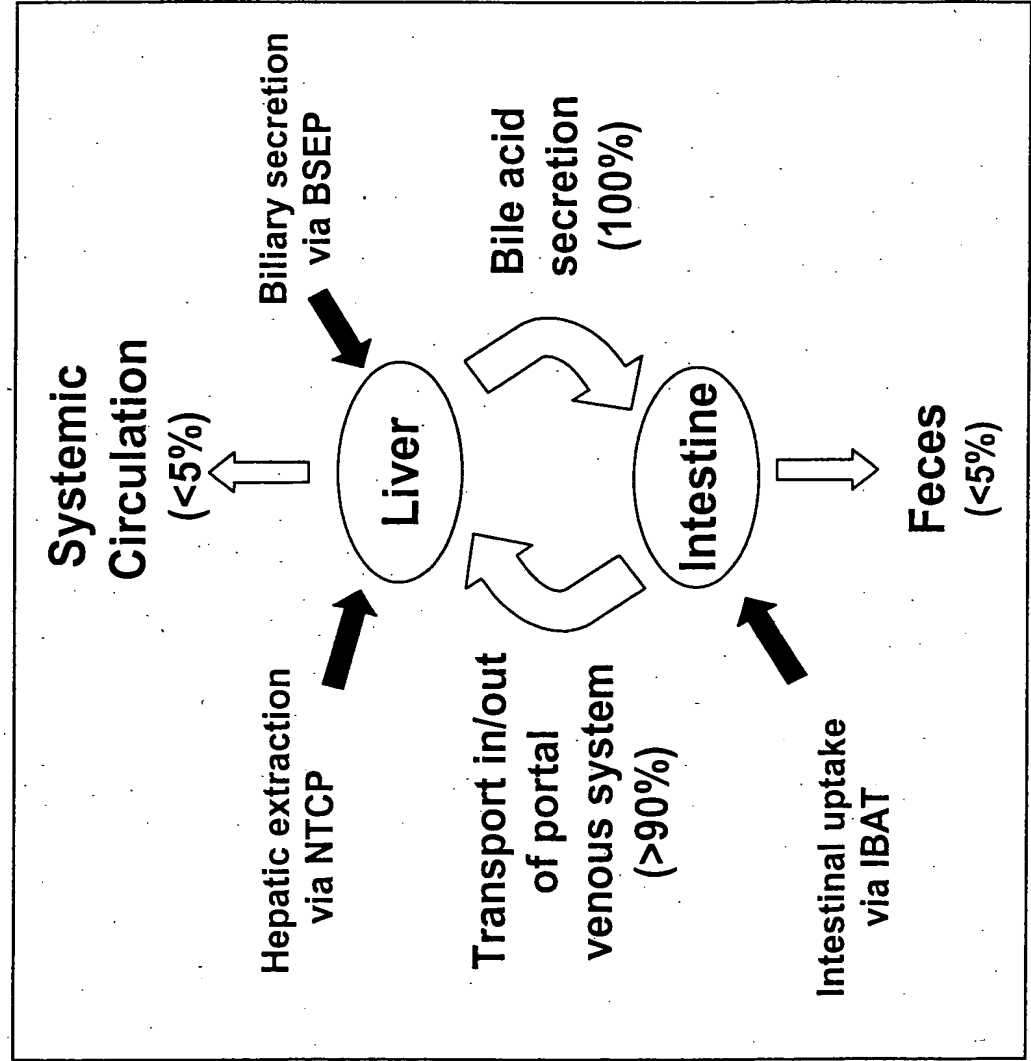


Figure 2

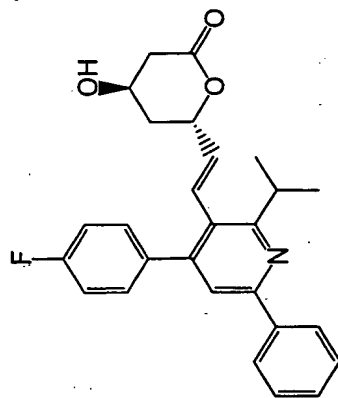
# The Enterohepatic Circulation with Key Transporter Proteins Mediating

## Bile Acid Circulation

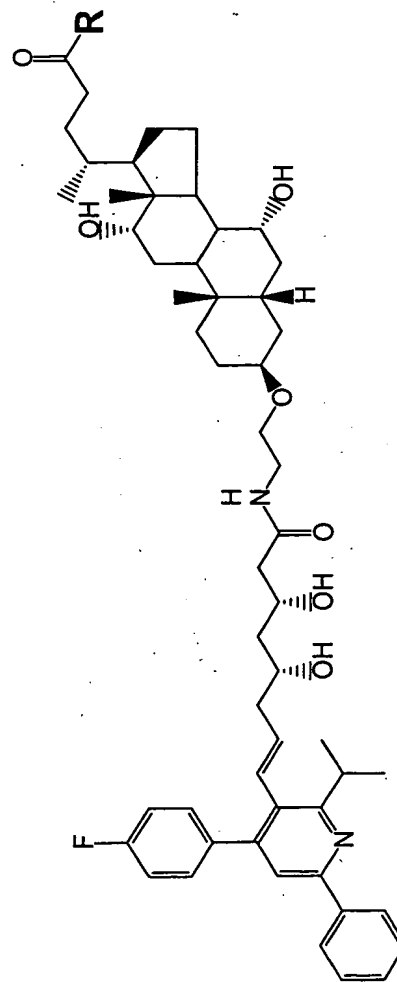


**Figure 3**

**Bile Acid Conjugates of HMG-CoA Reductase Inhibitor**



**HR 780**

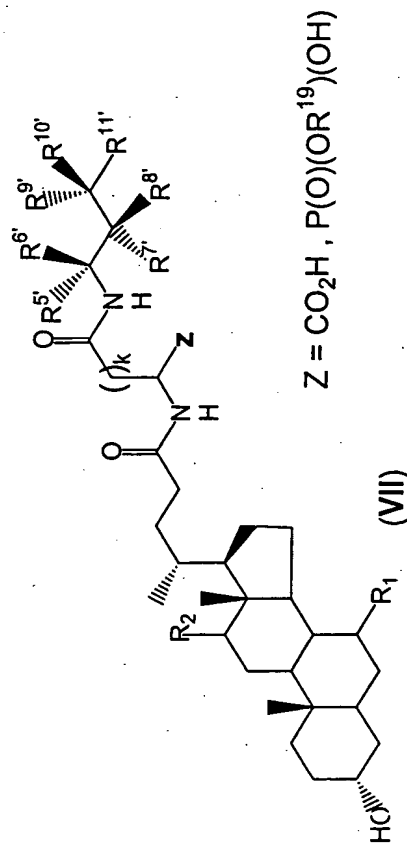
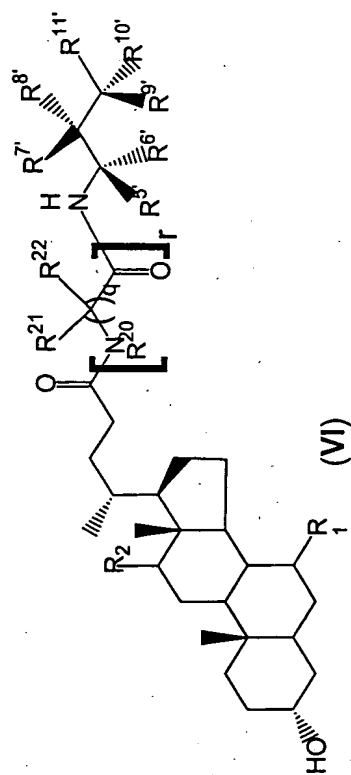
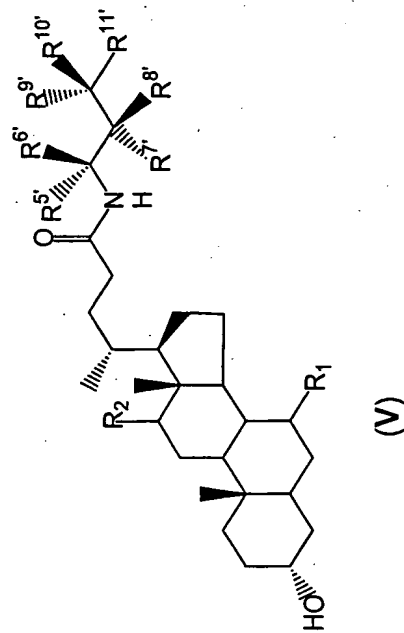


**R = OH S 3554**

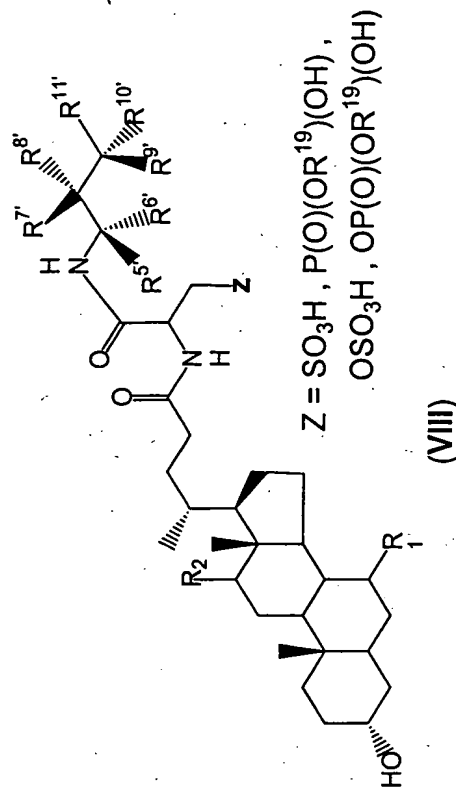
**R = NHCH<sub>2</sub>CO<sub>2</sub>H S 3898**

**R = NHCH<sub>2</sub>CH<sub>2</sub>SO<sub>3</sub>H S 4193**

Figure 4



Z = CO<sub>2</sub>H, P(O)(OR<sup>19</sup>)(OH)



Z = SO<sub>3</sub>H, P(O)(OR<sup>19</sup>)(OH),  
OSO<sub>3</sub>H, OP(O)(OR<sup>19</sup>)(OH)

- R<sub>1</sub> = α-OH ; R<sub>2</sub> = α-OH (Cholate)
- R<sub>1</sub> = β-OH ; R<sub>2</sub> = H (Ursodeoxycholate)
- R<sub>1</sub> = α-OH ; R<sub>2</sub> = H (Chenodeoxycholate)
- R<sub>1</sub> = H ; R<sub>2</sub> = α-OH (Deoxycholate)
- R<sub>1</sub> = β-OH ; R<sub>2</sub> = α-OH (Ursocholate)
- R<sub>1</sub> = H ; R<sub>2</sub> = H (Lithocholate)





Figure 7

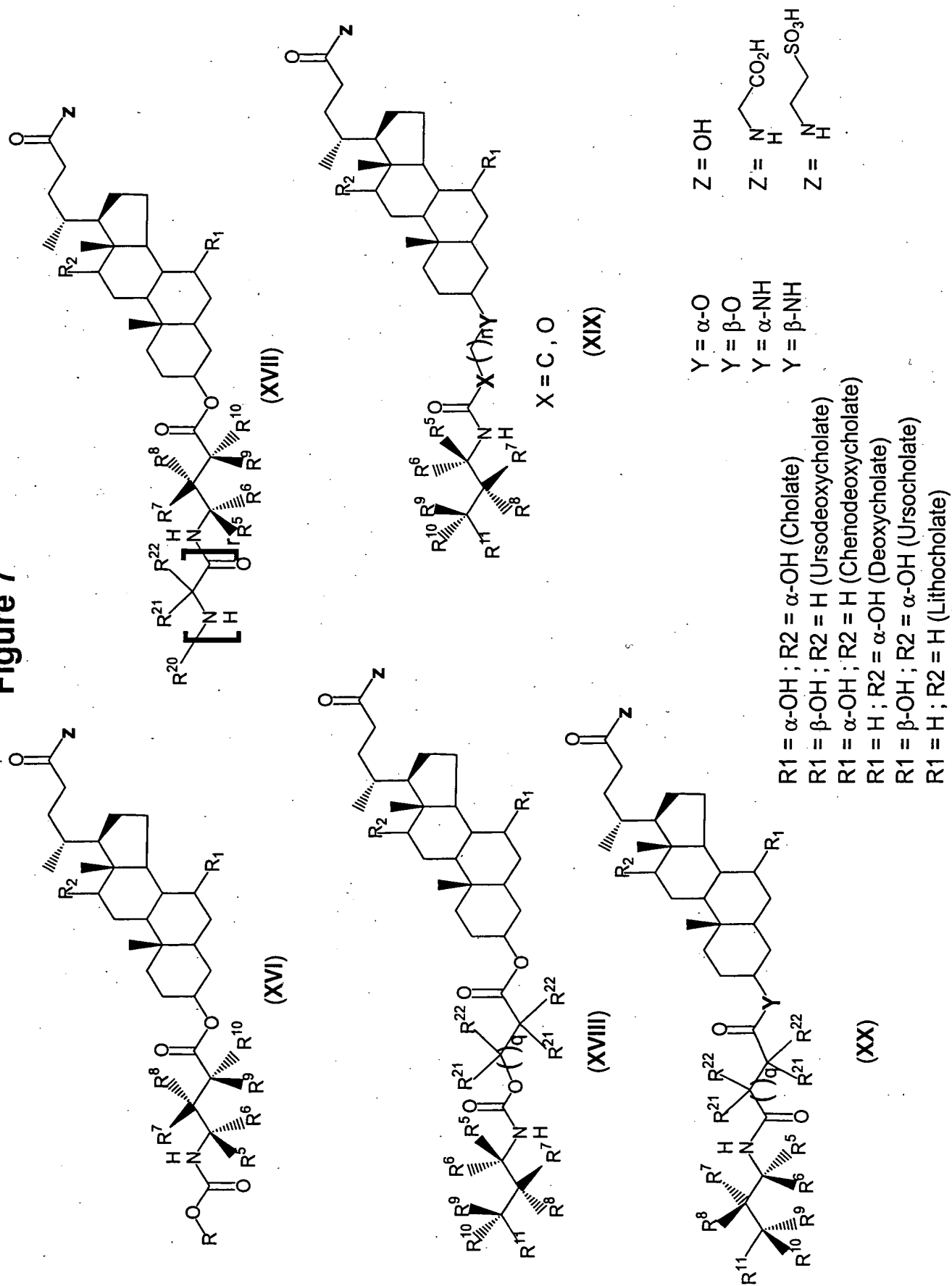
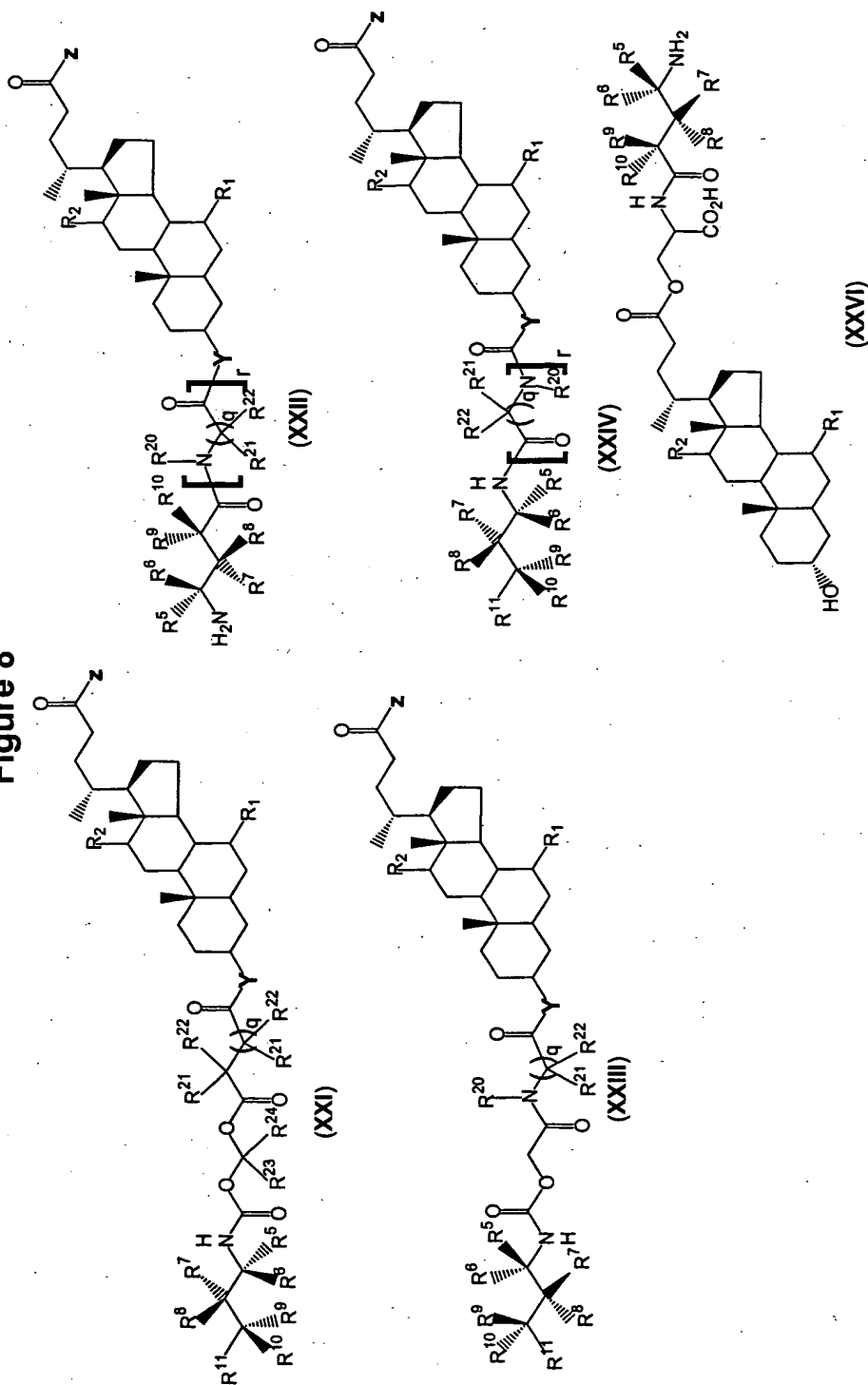


Figure 8



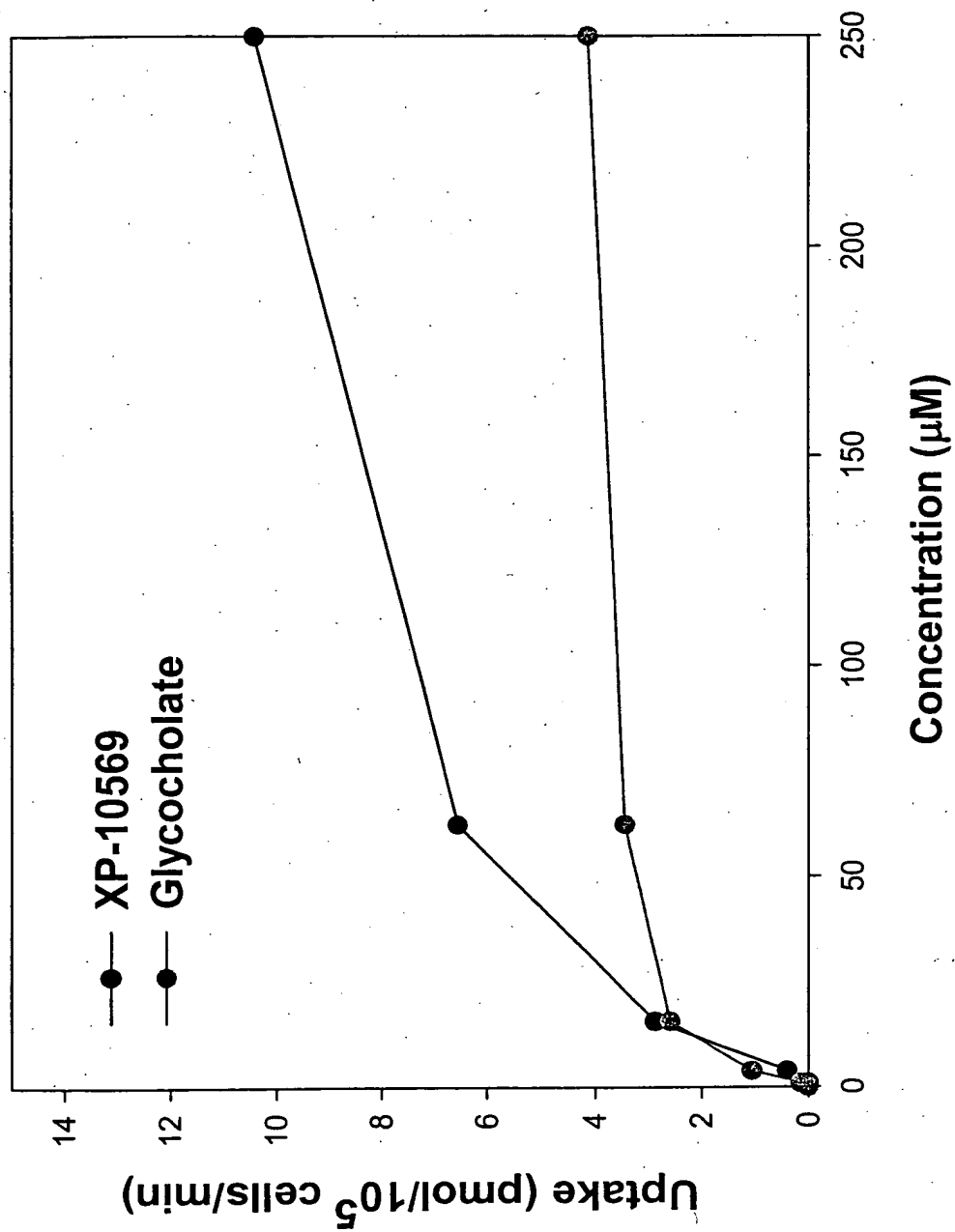
$R_1 = \alpha\text{-OH}$  ;  $R_2 = \alpha\text{-OH}$  (Cholate)  
 $R_1 = \beta\text{-OH}$  ;  $R_2 = H$  (Ursodeoxycholate)  
 $R_1 = \alpha\text{-OH}$  ;  $R_2 = H$  (Chenodeoxycholate)  
 $R_1 = H$  ;  $R_2 = \alpha\text{-OH}$  (Deoxycholate)  
 $R_1 = \beta\text{-OH}$  ;  $R_2 = \alpha\text{-OH}$  (Ursocholate)  
 $R_1 = H$  ;  $R_2 = H$  (Lithocholate)

$Y = \alpha\text{-O}$   
 $Y = \beta\text{-O}$   
 $Y = \alpha\text{-NH}$   
 $Y = \beta\text{-NH}$

$Z = OH$   
 $Z = N\text{-CH}_2\text{-CO}_2H$   
 $Z = N\text{-CH}_2\text{-SO}_3H$



**Figure 9: Uptake of (8) (XP10569) or Glycochocholate by IBAT-Transfected CHO Cells**



**Figure 10: Uptake of (8) (XP10569) or Glycocholate by  
LBAT-Transfected CHO Cells**

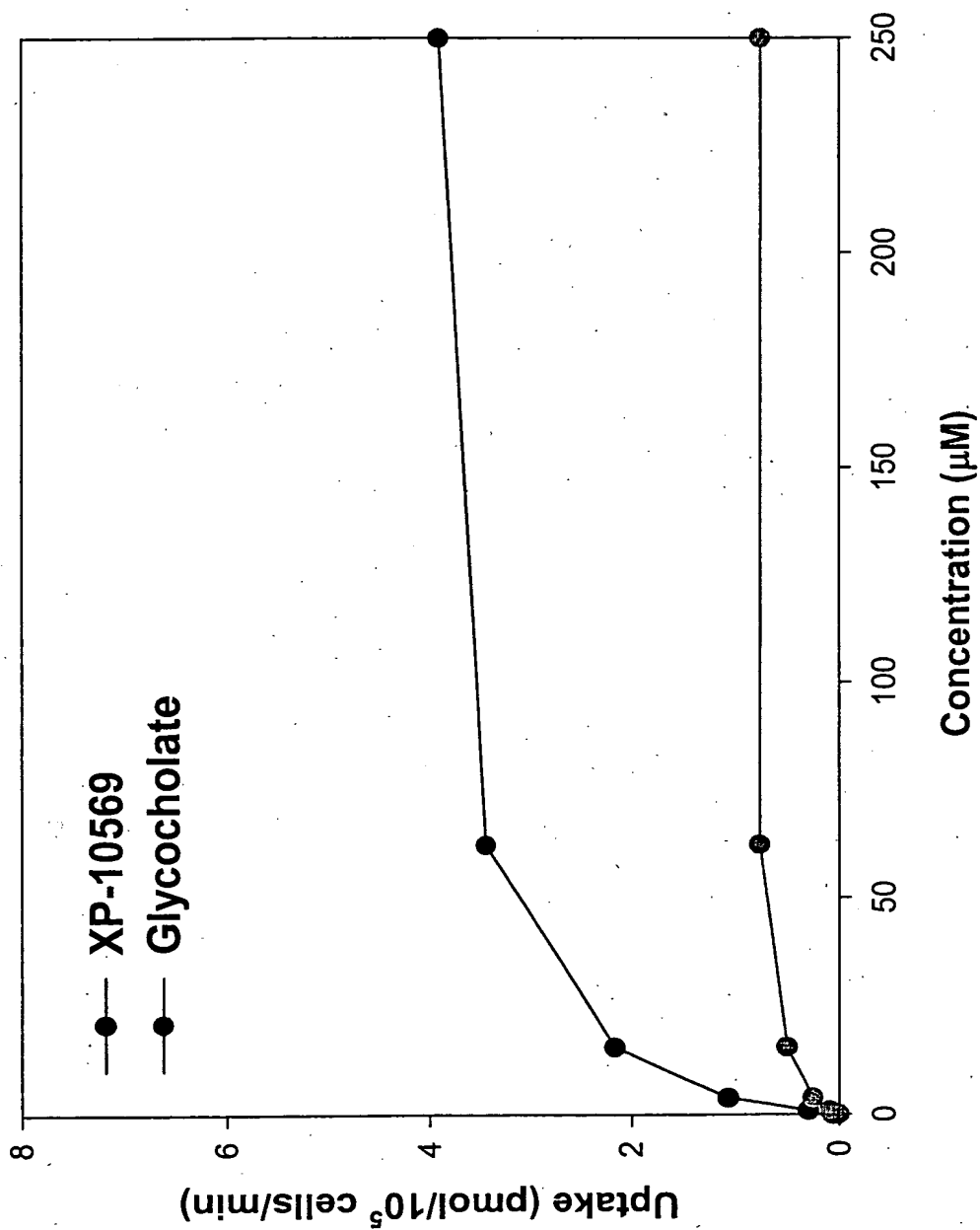


Figure 11

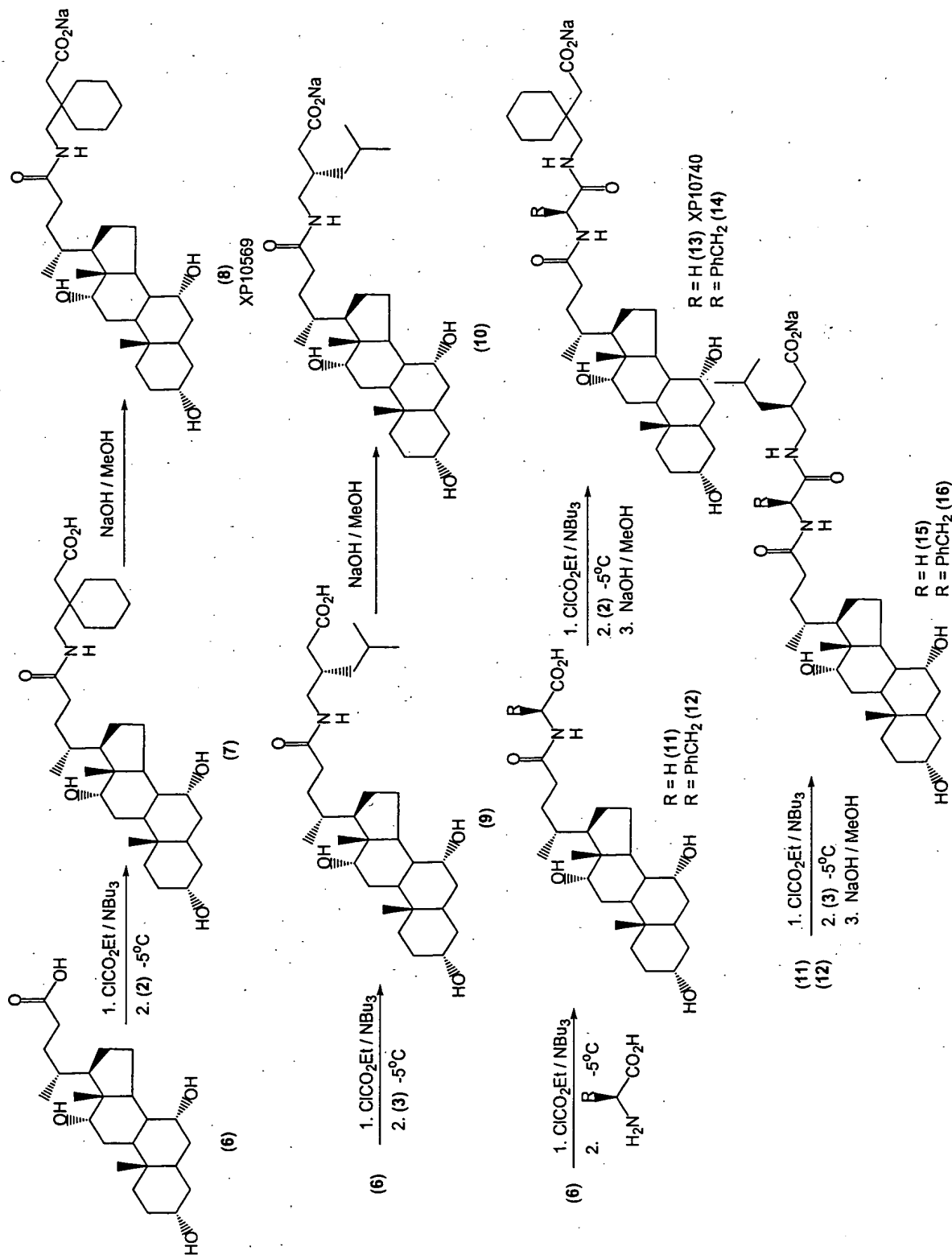








Figure 15

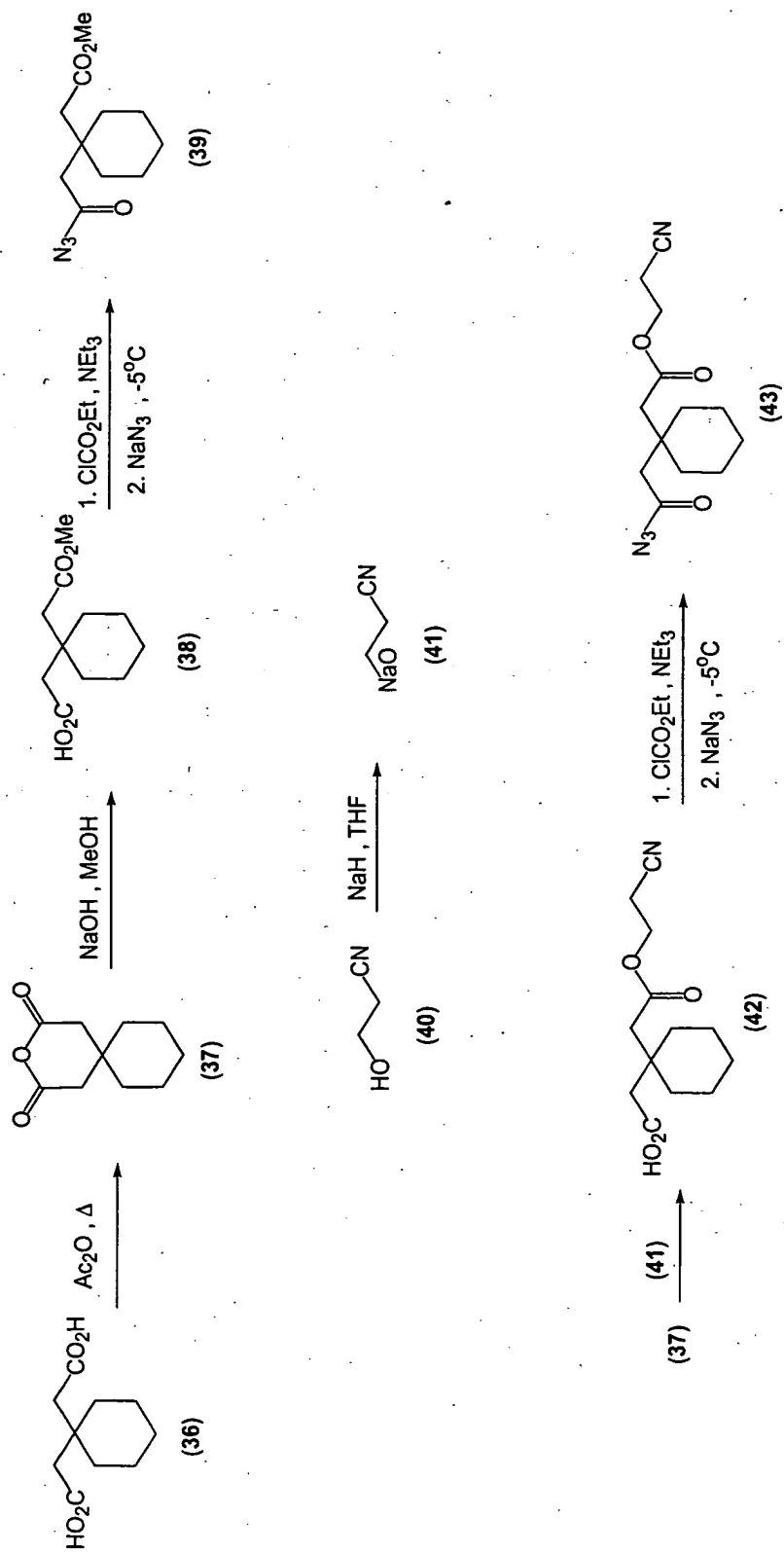


Figure 16

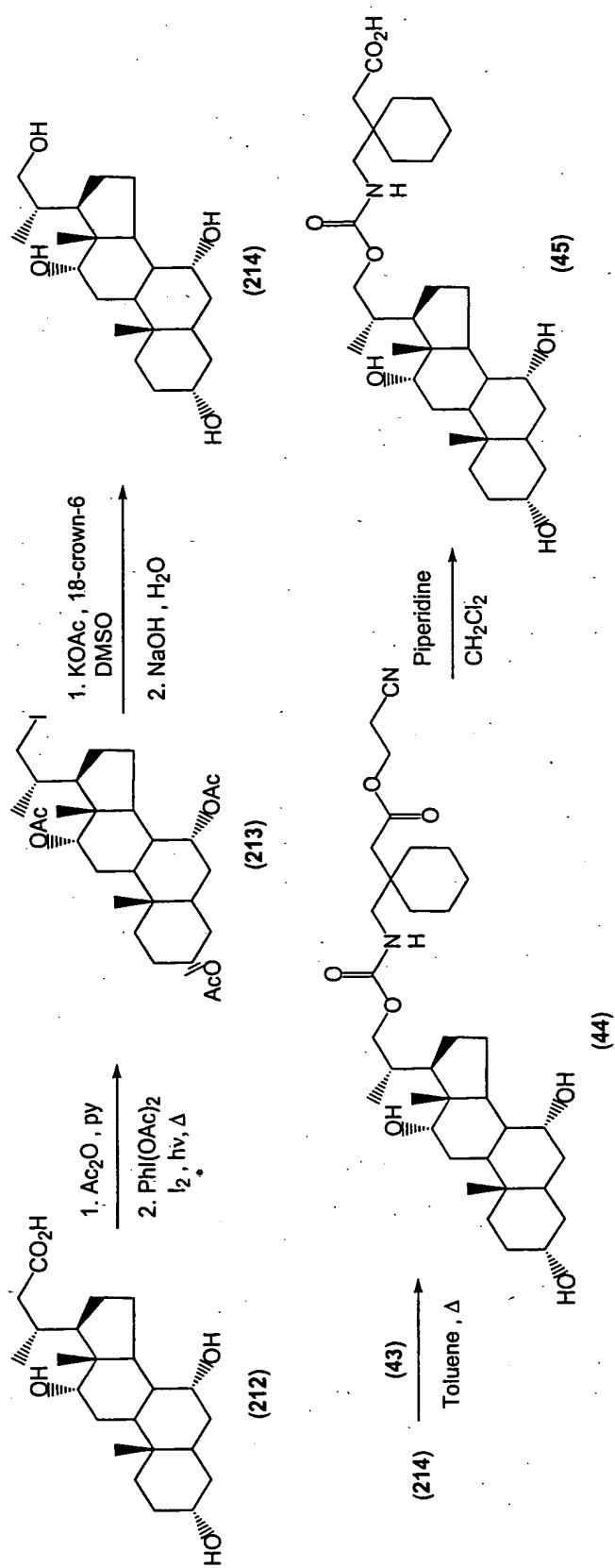




Figure 17

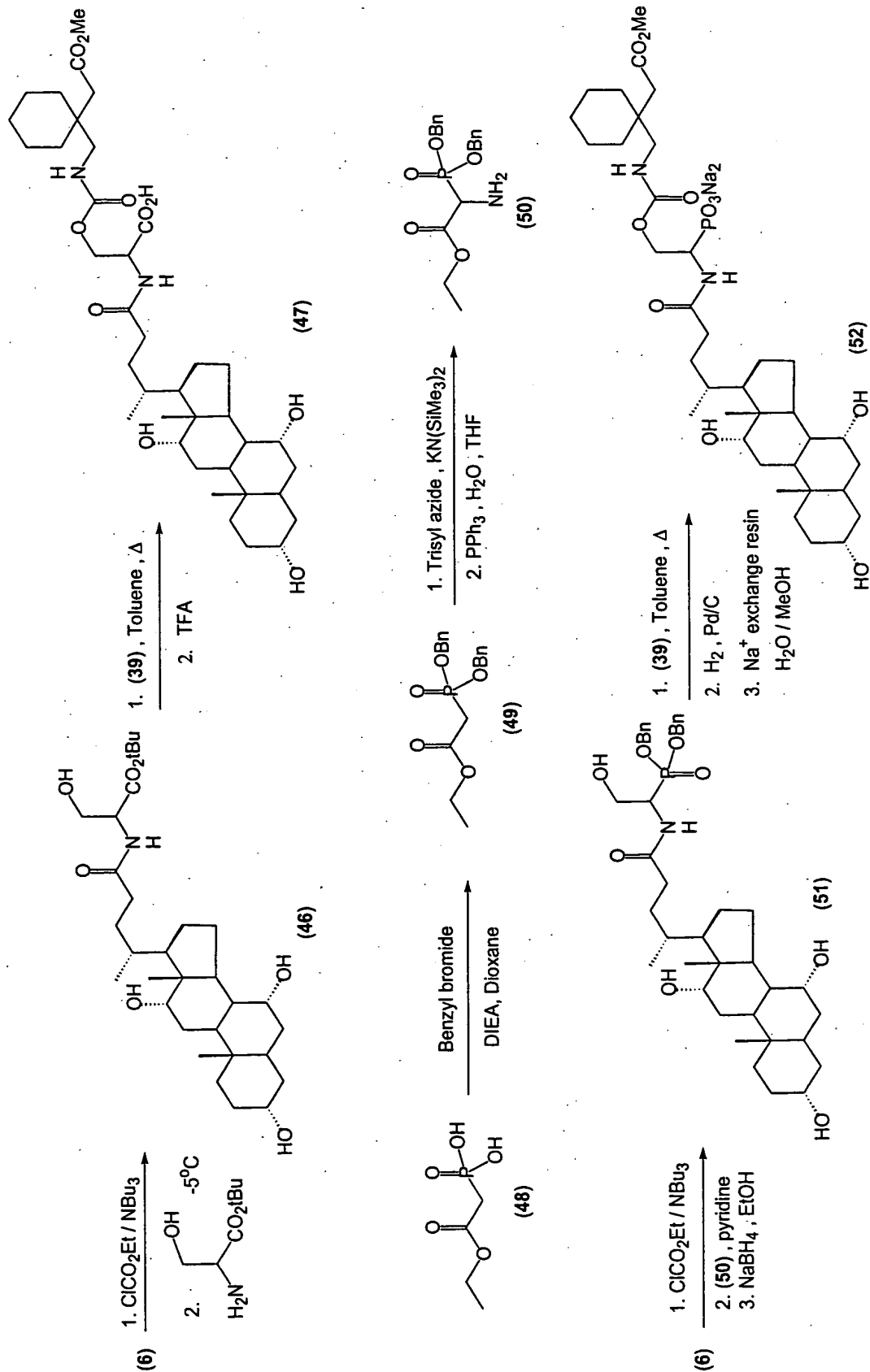


Figure 18

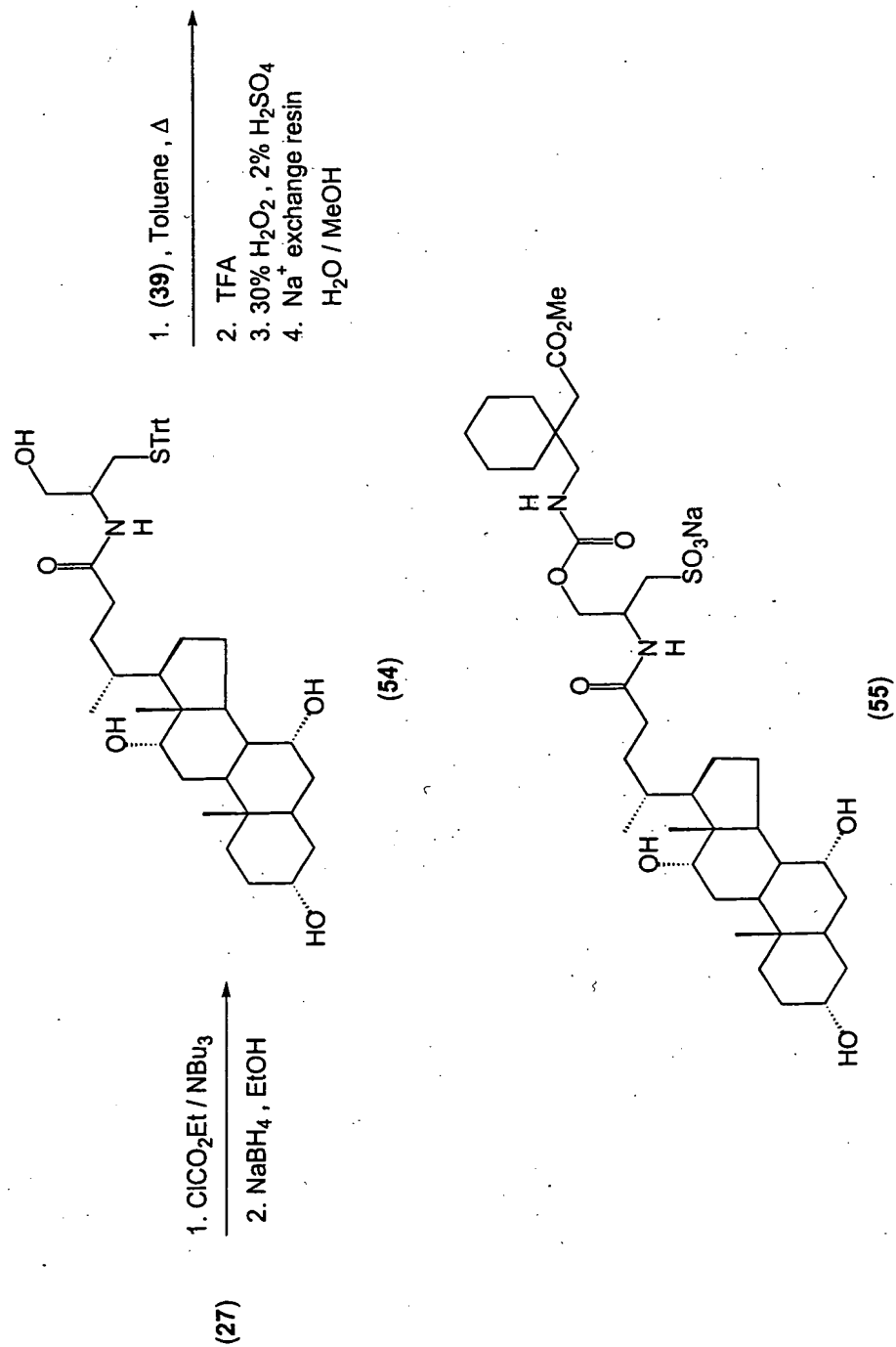


Figure 19

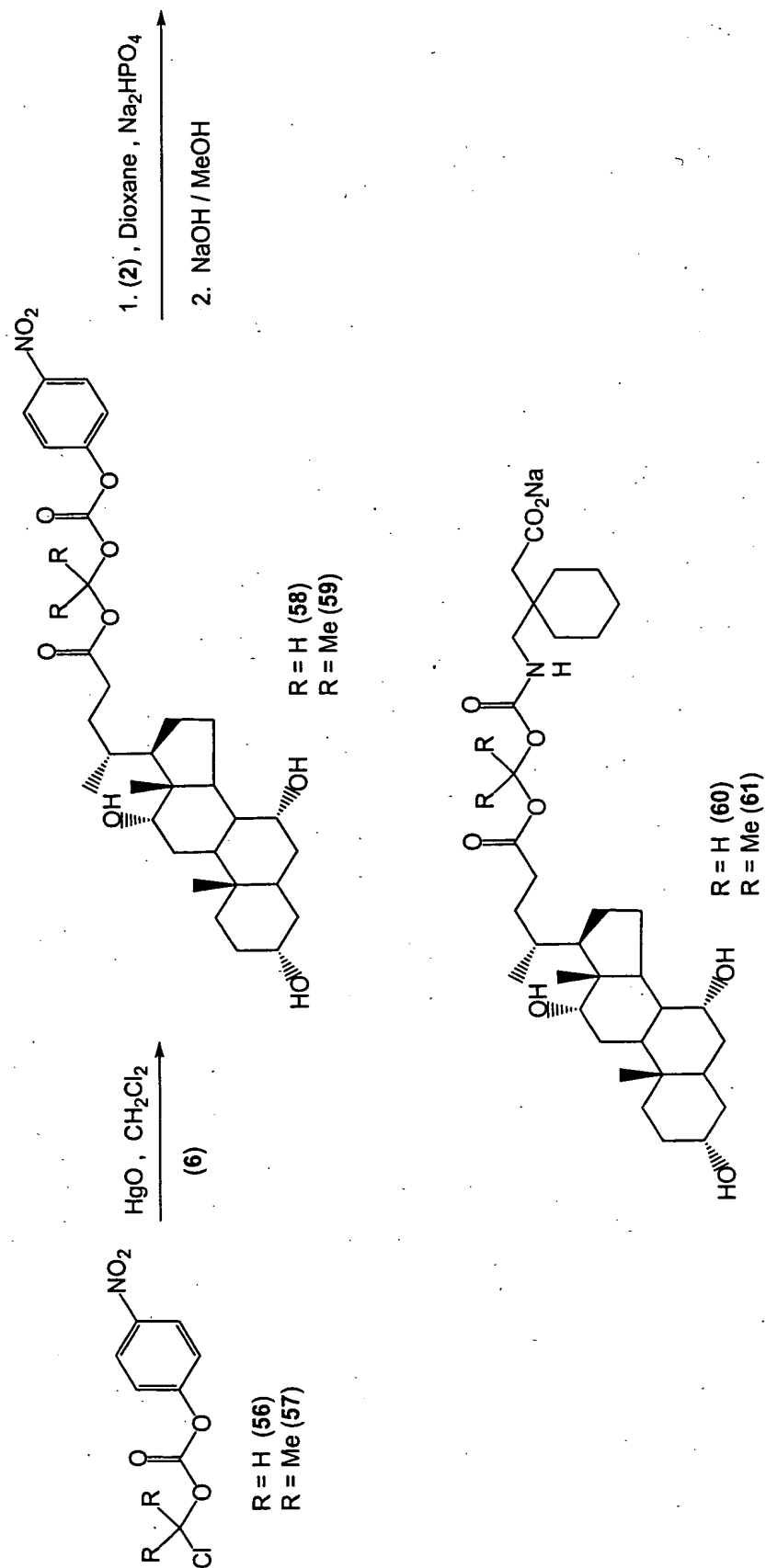




Figure 21

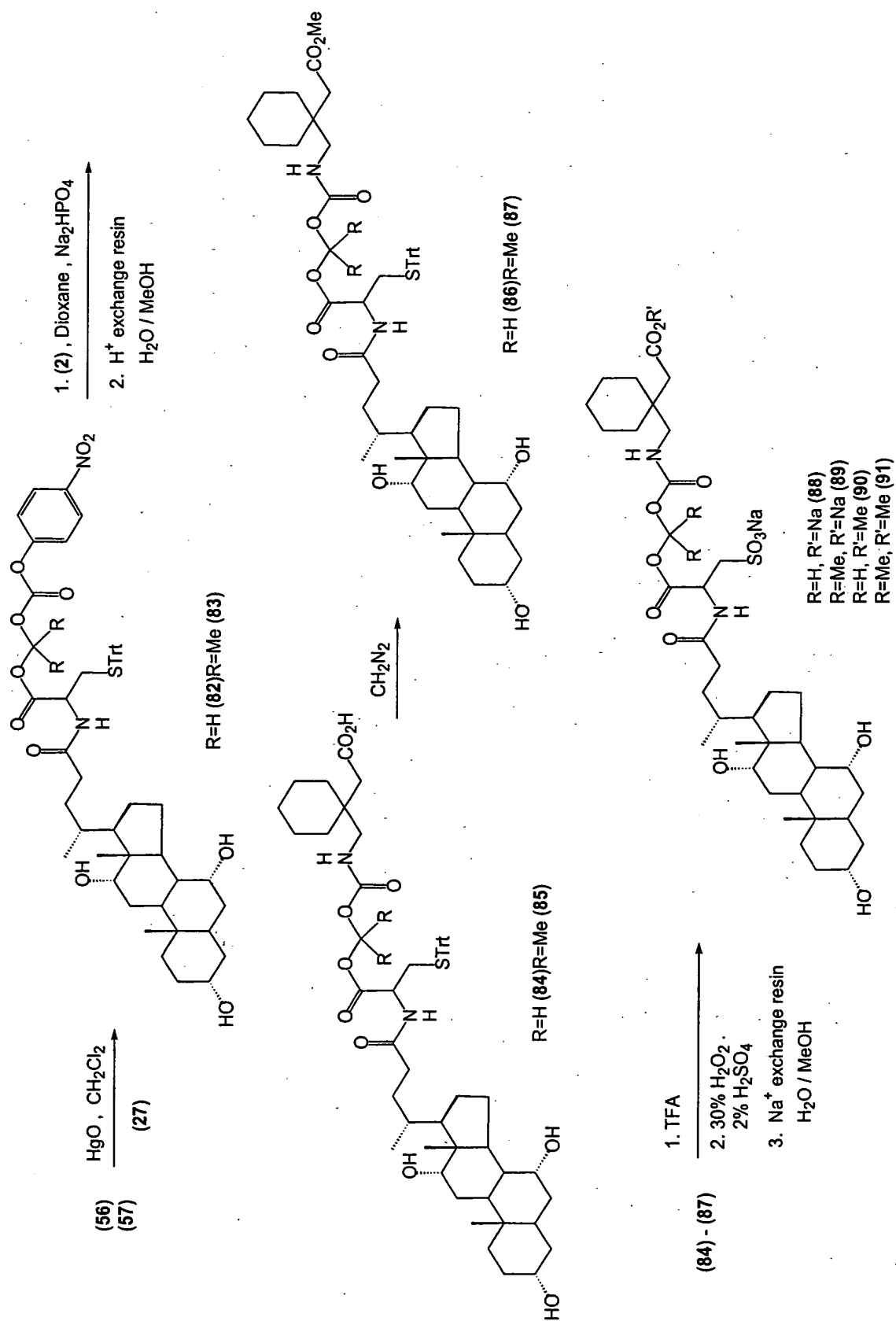
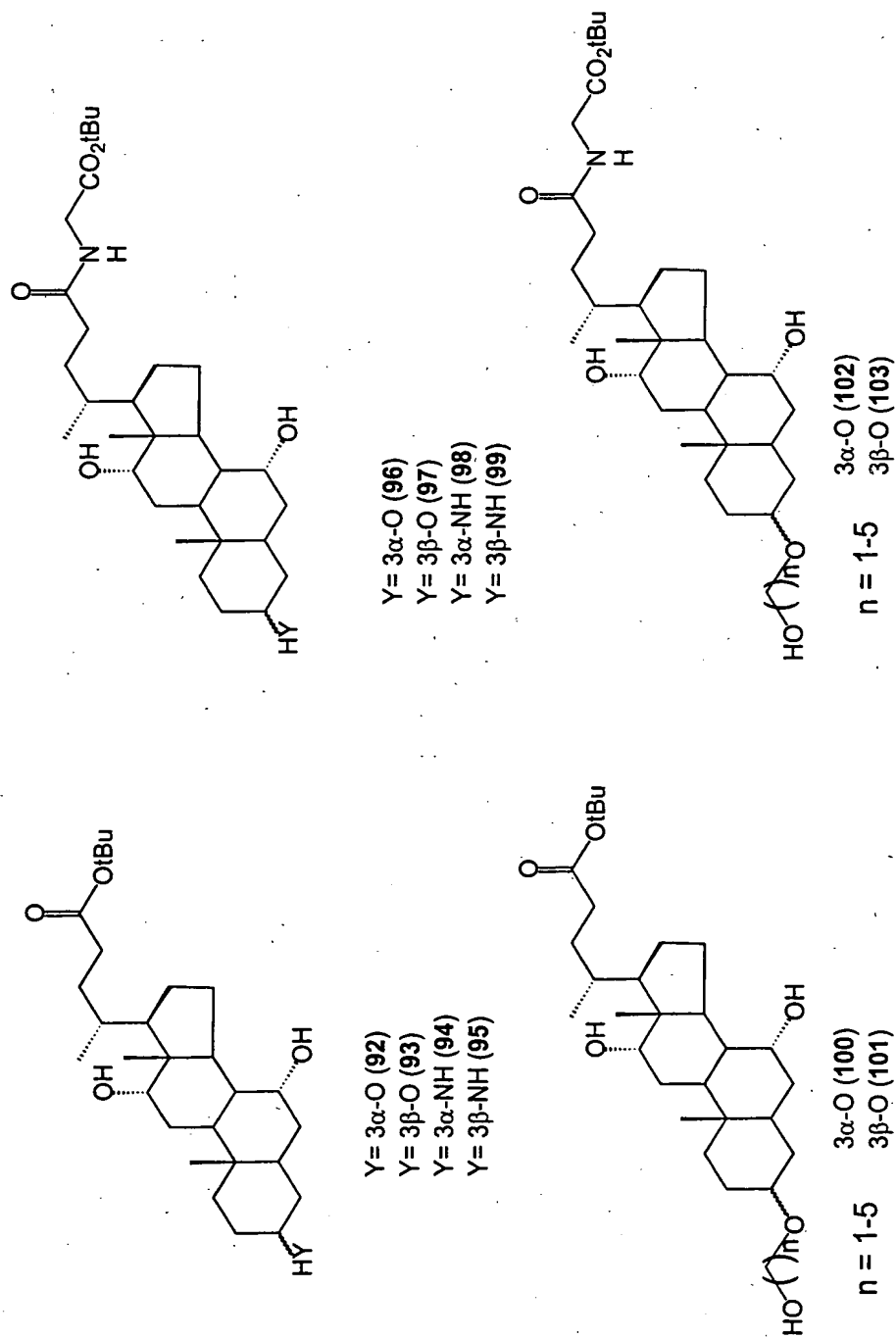


Figure 22



Compounds (92) - (103) prepared following methods described in co-pending application "Bile Acid-Derived Compounds for Enhancing Oral Absorption and Systemic Bioavailability of Drugs" assigned to XenoPort, Inc.

Figure 23

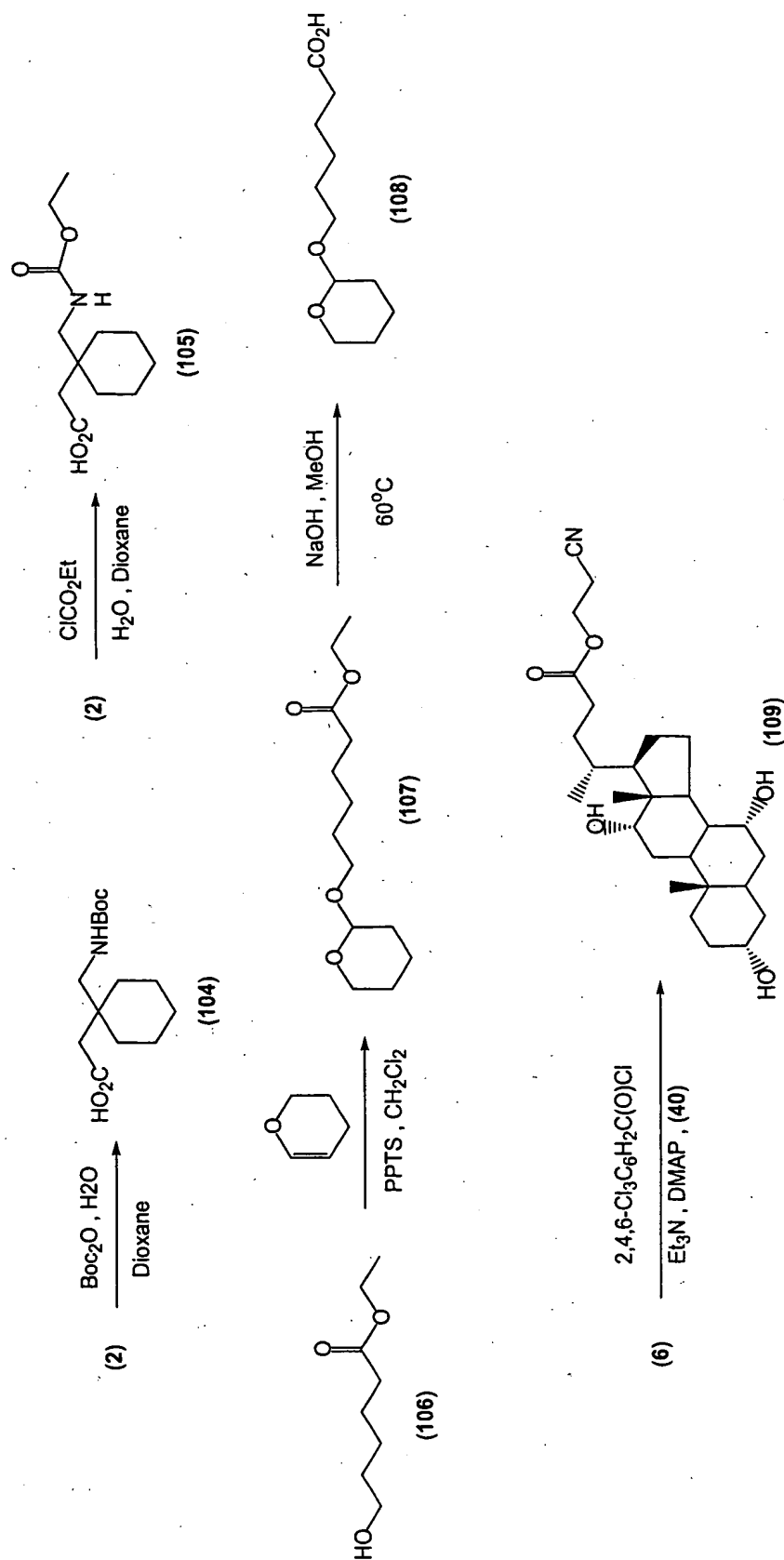


Figure 24

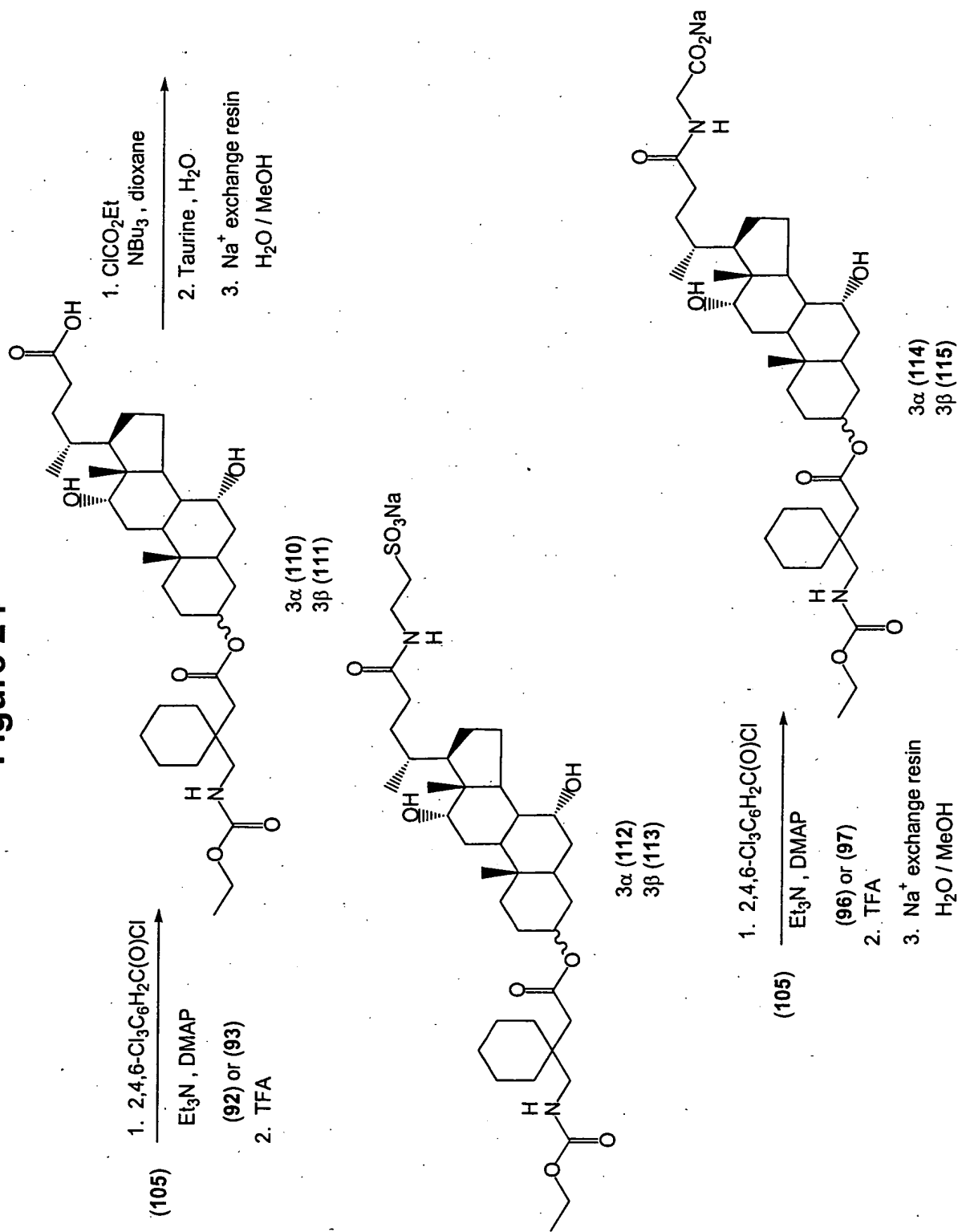






Figure 26

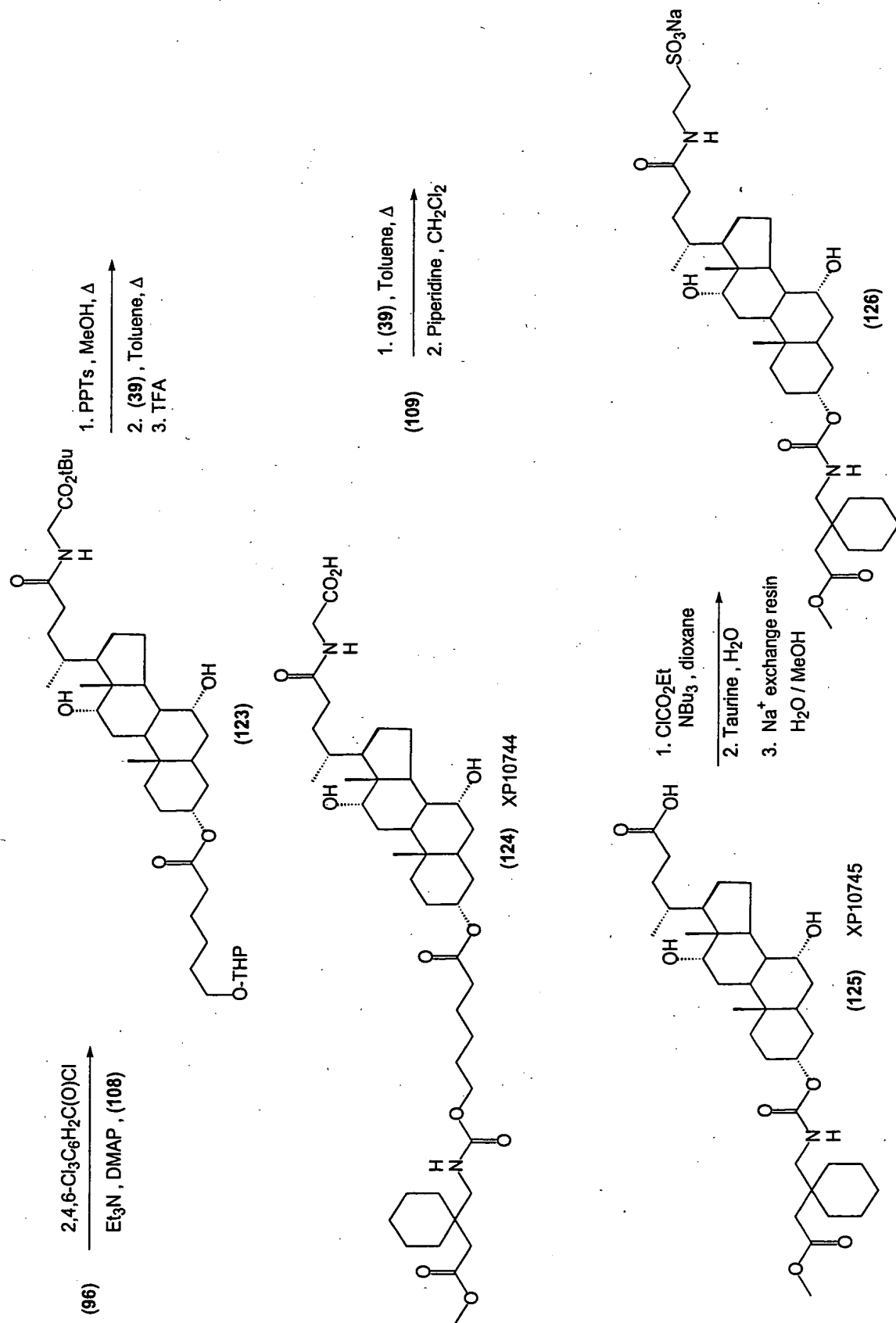


Figure 27

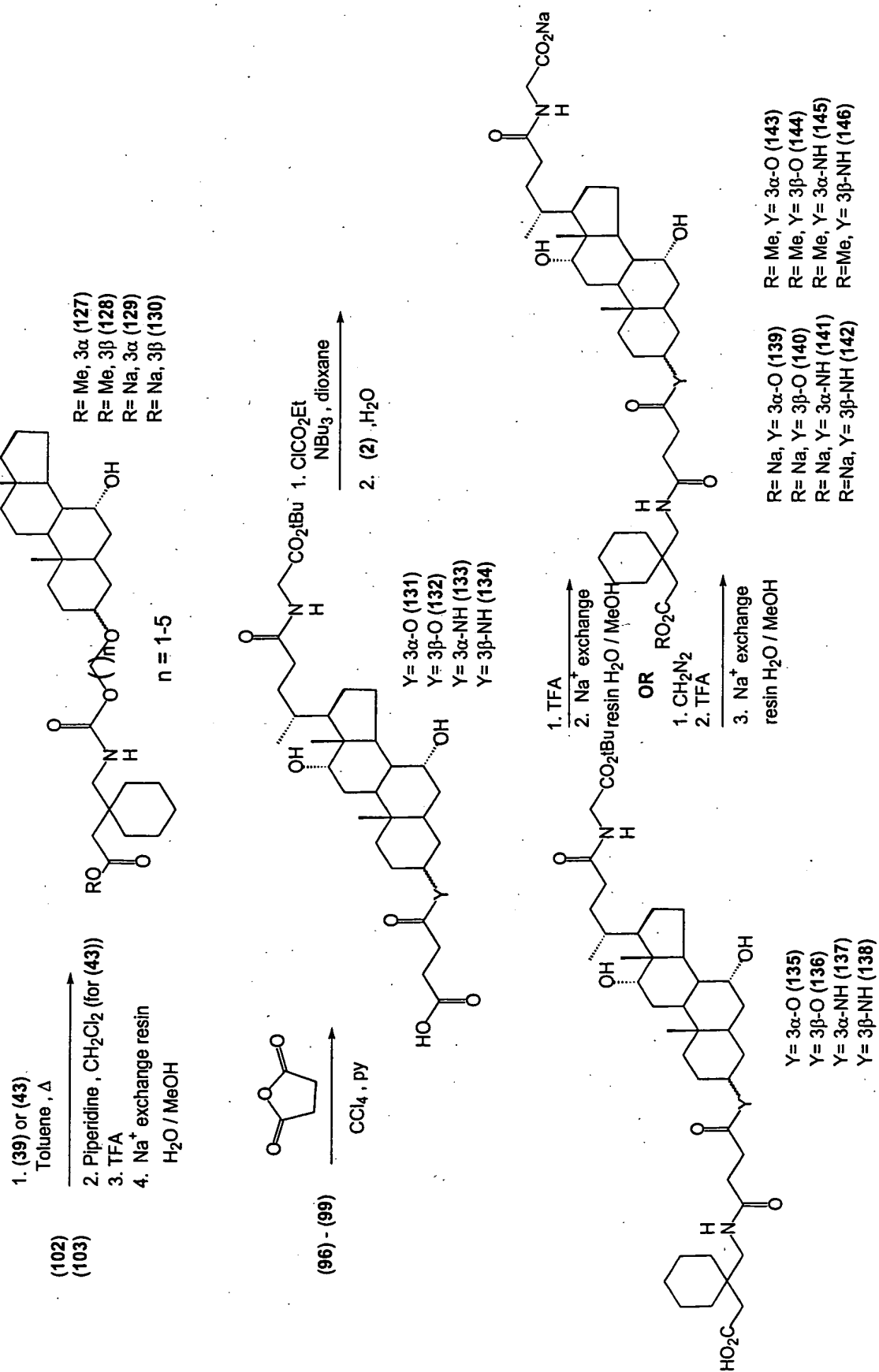
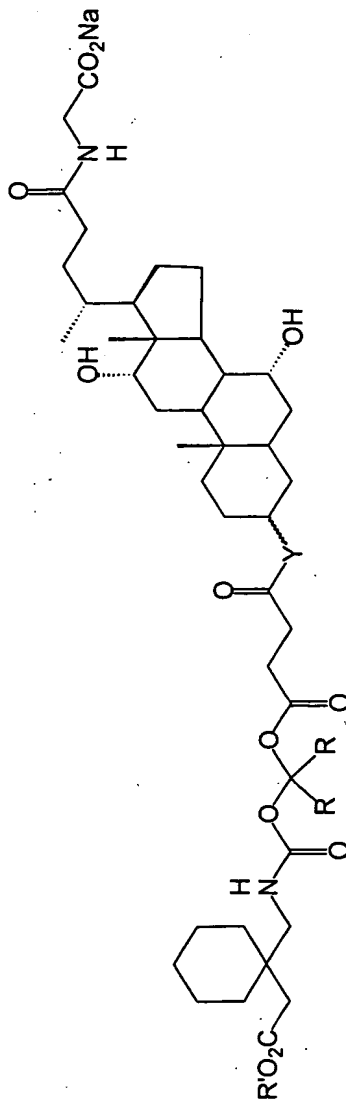
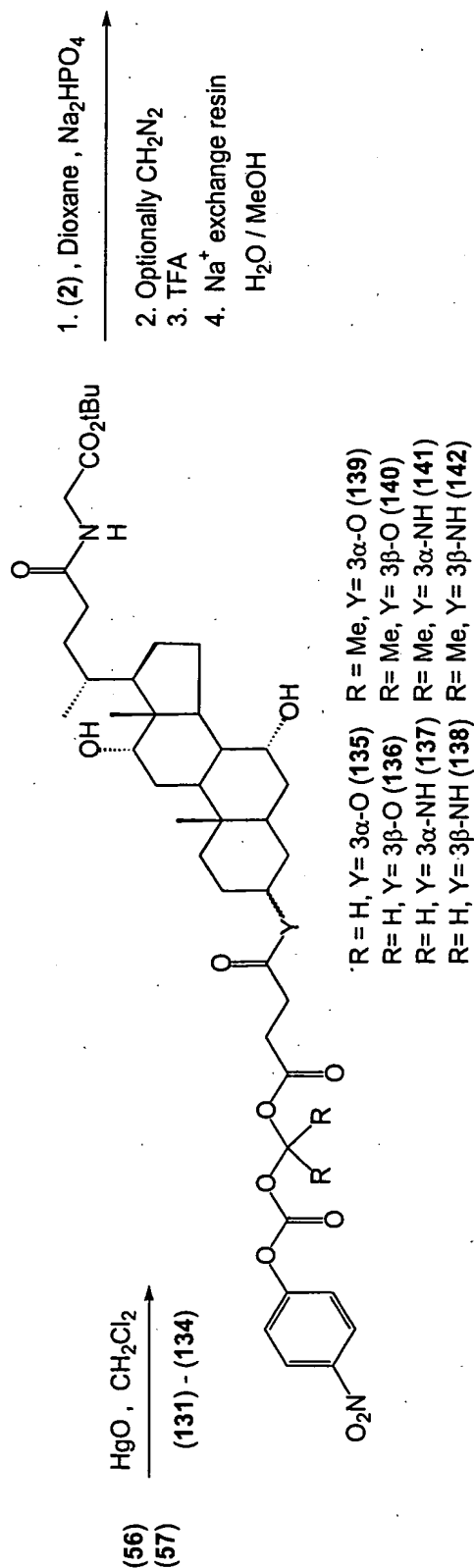


Figure 28



R' = Na, R = H, Y =  $3\alpha\text{-O}$  (143) R' = Na, R = Me, Y =  $3\alpha\text{-O}$  (147) R' = Me, R = H, Y =  $3\alpha\text{-O}$  (151) R' = Me, R = Me, Y =  $3\alpha\text{-O}$  (155)  
 R' = Na, R = H, Y =  $3\beta\text{-O}$  (144) R' = Na, R = Me, Y =  $3\beta\text{-O}$  (148) R' = Me, R = H, Y =  $3\beta\text{-O}$  (152) R' = Me, R = Me, Y =  $3\beta\text{-O}$  (156)  
 R' = Na, R = H, Y =  $3\alpha\text{-NH}$  (145) R' = Na, R = Me, Y =  $3\alpha\text{-NH}$  (149) R' = Me, R = H, Y =  $3\alpha\text{-NH}$  (153) R' = Me, R = Me, Y =  $3\alpha\text{-NH}$  (157)  
 R' = Na, R = H, Y =  $3\beta\text{-NH}$  (146) R' = Na, R = Me, Y =  $3\beta\text{-NH}$  (150) R' = Me, R = H, Y =  $3\beta\text{-NH}$  (154) R' = Me, R = Me, Y =  $3\beta\text{-NH}$  (158)

Figure 29

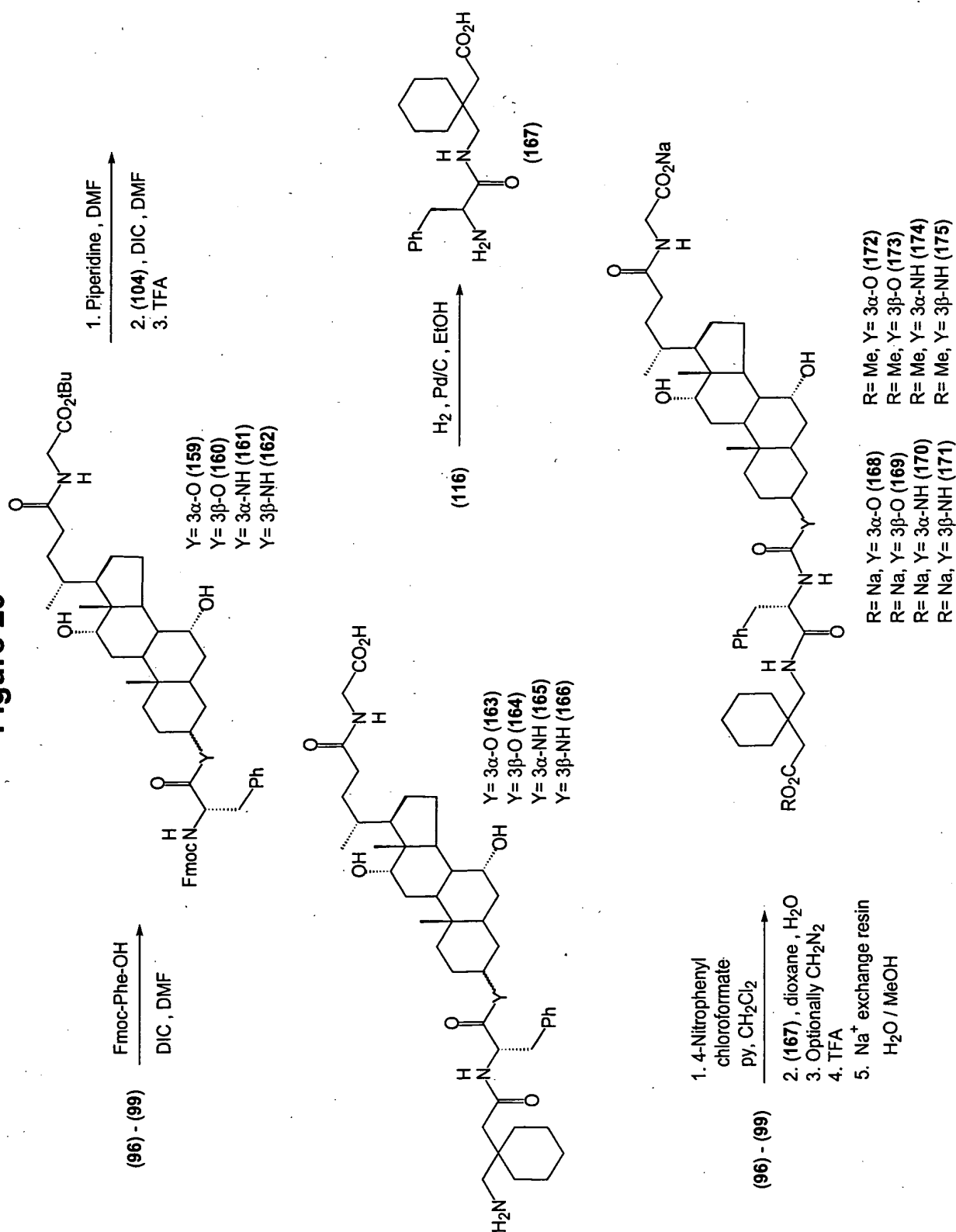


Figure 30

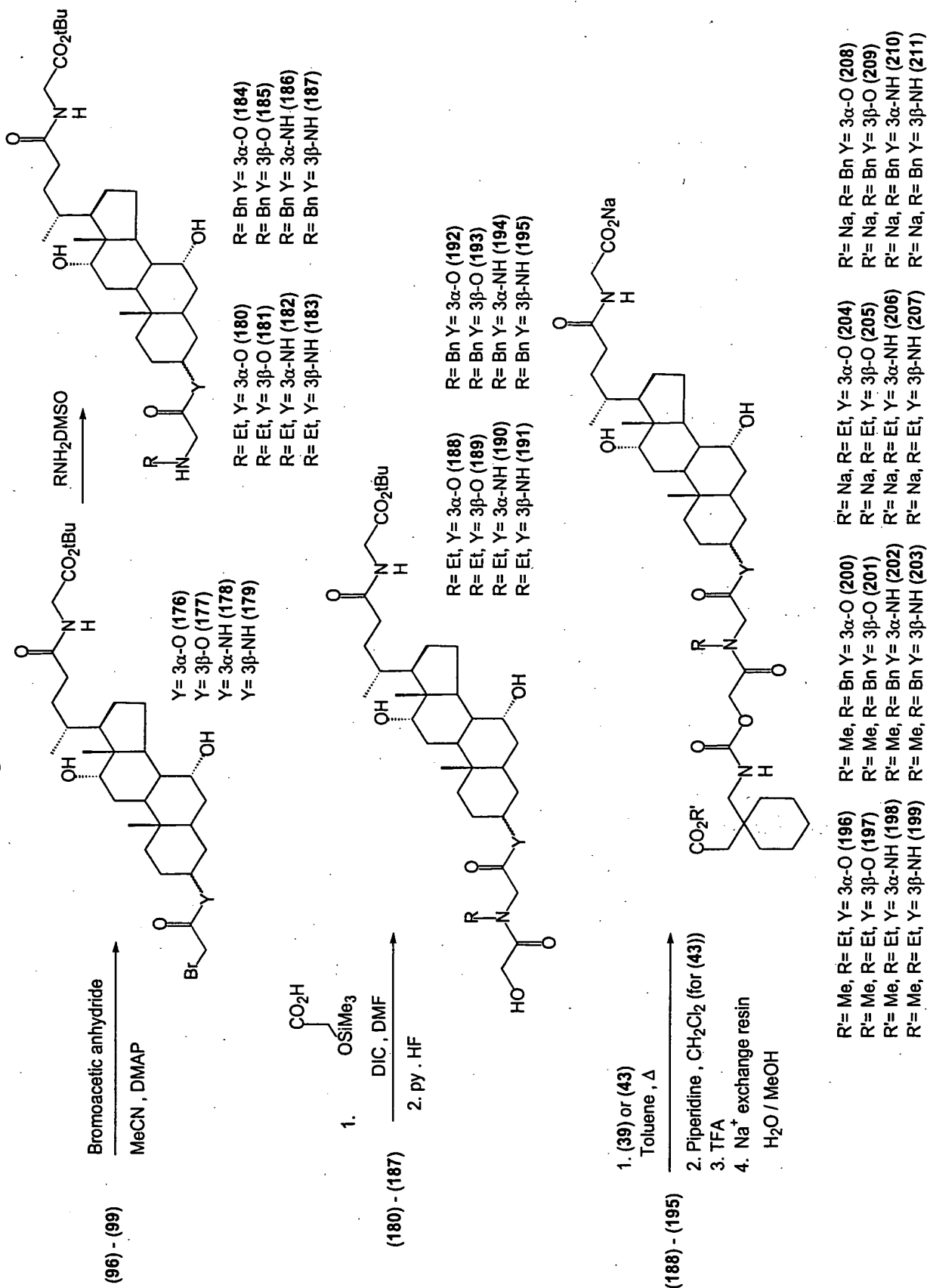
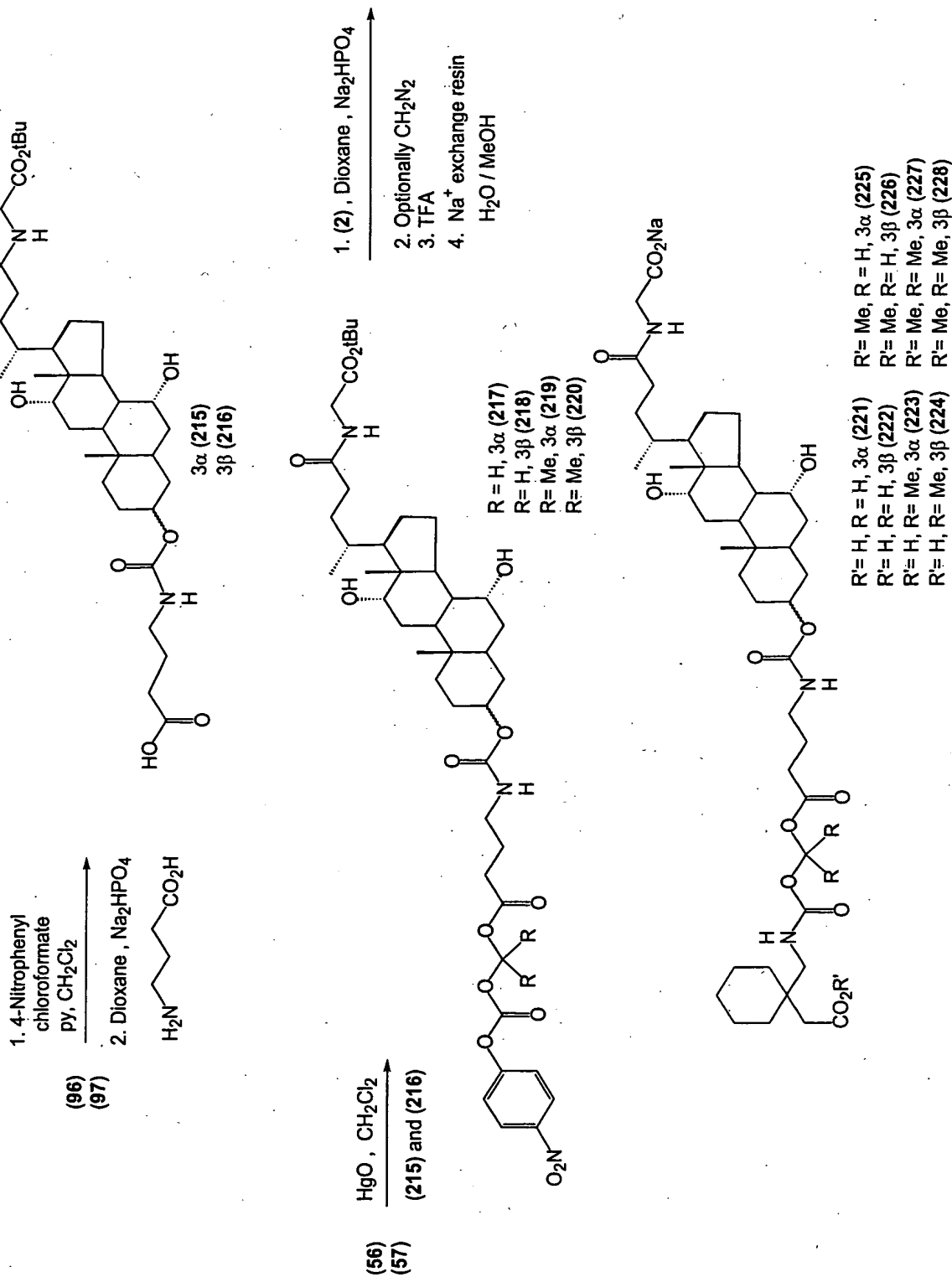


Figure 31



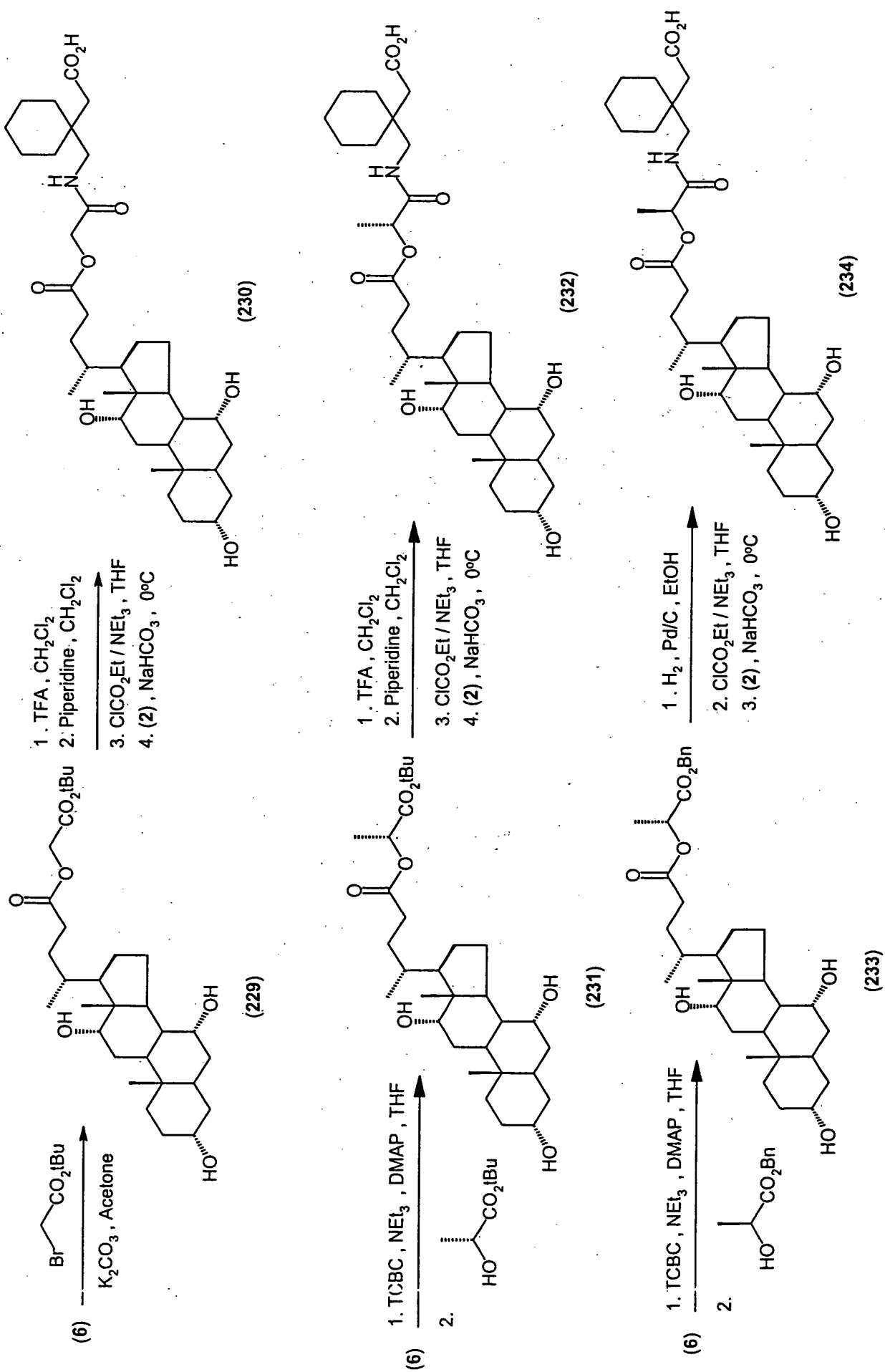




Figure 33

